

Large-scale production of lentiviral vector in a closed system hollow fiber bioreactor.

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Public Summary:

Lentiviral vectors are widely used in the field of gene therapy as an effective method for permanent gene delivery. While current methods of producing small scale vector batches for research purposes depend largely on culture flasks, the emergence and popularity of lentiviral vectors in translational, preclinical and clinical research has demanded their production on a much larger scale, a task that can be difficult to manage with the numbers of producer cell culture flasks required for large volumes of vector. To generate a large scale, partially closed system method for the manufacturing of clinical grade lentiviral vector suitable for the generation of induced pluripotent stem cells (iPSCs), we developed a method employing a hollow fiber bioreactor traditionally used for cell expansion. We have demonstrated the growth, transfection, and vector-producing capability of 293T producer cells in this system. Vector particle RNA titers after subsequent vector concentration yielded values comparable to lentiviral iPSC induction vector batches produced using traditional culture methods in 225 cm² flasks (T225s) and in 10-layer cell factories (CF10s), while yielding a volume nearly 145 times larger than the yield from a T225 flask and nearly three times larger than the yield from a CF10. Employing a closed system hollow fiber bioreactor for vector production offers the possibility of manufacturing large quantities of gene therapy vector while minimizing reagent usage, equipment footprint, and open system manipulation.

Scientific Abstract:

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